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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
GUCKER, S	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Part III DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1645.

2. Since this application is eligible for the transitional procedure of 37 CFR 1.129(a), and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action is hereby withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on 1/29/98 has been entered.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Any objections or rejections made in a previous Office Action that are not herein reinstated have been withdrawn.

5. The disclosure is objected to because of the following informalities: the address of the ATCC recited in the specification is no longer valid. The current address is: American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209.

The status of U.S.S.N. 08/167,109 in the first sentence of the specification should be updated.

Appropriate correction is required.

6. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the

following is required: the phrase "a recombinant nucleic acid" is not found in the specification, although it is found in claim 1 as originally filed.

7. 35 U.S.C. 101 reads as follows:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.**

Claims 9 and 10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The term "recombinant" does not distinguish the nucleic acid so described as being chemically different from nucleic acid found naturally in cells, therefore the claims read on a product of nature. A recombinant nucleic acid can be composed of a nucleotide sequence identical to an unisolated or unpurified nucleotide sequence found in nature which does not show the hand of man.

8. Claims 8-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contains reference to a deposit known as ATCC 75949. It does not refer to a deposit known as ATCC 97525, as recited in the instant claims. This is a new matter rejection.

Claims 9 and 10 recite "enhances [a] neuronal regeneration process" and were not originally filed. The Applicant has not identified support for such new claim language in the

specification and the claims are rejected as containing new matter. It is noted that page 4, lines 5-7 read in part "...promotion of the regeneration of a process of a central or peripheral neuron."

9. Claims 9-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant specification describes the purification of partial nucleic acids encoding partial amino acid sequences of a single protein species, protein 68075, from a single animal species, human. The specification therefore has a single embodiment that has been shown to work as a transcription factor *in vitro*. It does not adequately describe, give examples, or provide guidance on the purification of nucleic acids from any other animal species or different forms of nucleic acids from the same species that would function as transcription factors because the term "stringent" which is not specifically defined in the disclosure encompasses all degrees of stringency, from low to high stringency and all intermediate stringencies. In other words, the term "stringency" is a relative term open to modification such as "low" stringency" (relatively large number of embodiments) or "high" stringency (relatively lower number of embodiments). In addition, the precise temperature, number of washings, ionic strength, etc. that comprise "stringent" conditions for hybridization (of any degree, low, high, etc.) as compared to non-stringent conditions are not described in sufficient detail or specificity in either the claims or the specification to limit the number of embodiments, so the claims encompass an infinite variety of

nucleic acids that possess little structural similarity to the partial nucleic acid encoding part of protein 68075, and therefore the vast majority of the resultant encoded proteins would not share the functional properties of the amino acid sequence encoded by the deposited clone and therefore the artisan could not use the vast majority of encompassed hybridizing nucleic acids with any reasonable expectation of success. Because the specification only discloses a single embodiment which is not reasonably predictive of either the structure or function of the infinite number of nucleic acids that stringently hybridize to it, undue experimentation would be required to enable hybridizing nucleic acids, if any, that encoded a protein that the skilled artisan could use with a reasonable expectation of success. The instant teachings of the partial nucleic acids does not include any information as to the actual nucleotide sequence of the instant nucleic acids, the nucleotide sequence of nucleic acids from other animal species, or the nucleotide sequence of nucleic acids that hybridize under stringent conditions with the partial nucleic acid that encodes part of protein 68075. Applicant has set forth only functional properties of the claimed genus of hybridizing nucleic acids of instant claim 9 without any structural properties to distinguish that genus. The disclosure does not provide sufficient guidance or examples to enable the chemical genus of claim 9 in the absence of any and all structural limitations.

As taught by the specification (page 5, lines 23-31), it is the encoded protein that possesses the functional property of enhancing the regeneration of a nerve cell process and not the nucleic acid or fragment thereof encoding that protein. It is suggested that the claims be amended to refer to the encoded protein as possessing the functional property because the nucleic acids

themselves do not possess and are not enabled for the functional property recited. Should the grounds of this rejection be overcome, the following scope rejection would be applicable to claims 9-10.

10. Claims 9-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling (if all the grounds of the rejection of ¶9 set forth above are overcome) for a purified nucleic acid comprising Clone ATCC 75949 or a purified fragment of Clone ATCC 75949 that encodes a protein that promotes the regeneration of a process of a central or peripheral neuron *in vitro*, does not reasonably provide enablement for a recombinant nucleic acid that hybridizes with Clone ATCC 97525 or a fragment of Clone ATCC 97525 and enhances [a] neuronal regeneration process. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The disclosure does not contain an adequate written description, examples, or guidance to enable language such as "enhances [a] neuronal regeneration process" because this language encompasses *in vivo* use. In order for an encoding nucleic acid to be even remotely considered to possess such a functional property, it would have to be expressed and translated into a protein in the neuron that required regeneration because it is the protein itself, and not the encoding nucleic acid, that possesses the functional property of neuronal regeneration (see page 5, lines 23-31 of specification). Obstacles to application of nucleic acid drugs *in vivo* are provided by the review of Stull et al. (pages 476-478). Applicant has supplied information on the record asserting that

protein 68075 may also be known as transcription factor MEF2C. Transcription factors are proteins that function internally in a cell by binding to DNA in the nucleus. Transcription factors do not work when applied externally to a cell because they do not cross the cell membrane and cannot reach the DNA in the nucleus. Applicant has admitted on the record that he does not claim to have done experiments on human beings (Paper No. 15, filed 1/29/98, page 4). The specification does not contain any working embodiments of animal experiments. The 1.132 declaration of Dr. Krainc indicates that MEF2C gene, also known as clone TR2B, also known as ATCC 75949, also known as a nucleic acid partially encoding protein 68075, when transfected into F19 EC cells *in vitro*, allows the labeling of neurofilaments by antibodies. Dr. Krainc interprets this antibody labeling as being important for neuronal regeneration. However, transfection means that the nucleic acid had to be delivered internally to the cells *in vitro* across the cell membrane, then utilized by the cells to produce the biologically active protein 68075. To accomplish the same results *in vivo* would mean that in order to practice the invention as claimed (enhances neuronal regeneration), gene therapy would have to be successfully performed. The disclosure does not provide a sufficient written description, examples, or guidance for gene therapy to be enabled for the following reasons. Gene therapy has not been performed to date with a reasonable expectation of success or predictability. For example, the 1995 "Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy" states that:

"While the expectations and the promise of gene therapy are great, clinical efficacy has not been definitely demonstrated at this time in *any gene therapy protocol*, despite anecdotal claims of

successful therapy and the initiation of more than 100 Recombinant DNA Advisory Committee (RAC)-approved protocols.

Significant problems remain in all basis aspects of gene therapy. Major difficulties at the basic level include *shortcomings in all current gene transfer vectors* and an *inadequate understanding of the biological interaction of these vectors with the host"* [emphasis added; page 1].

Therefore, the lack of working embodiments in the disclosure would force even those of the highest skill in the art to perform undue, not routine, experimentation in order to enable the invention as claimed. Additionally, neurons in the central nervous system do not exist in a supportive environment for their processes to regenerate and active inhibition of such regeneration occurs *in vivo* (see review by Jackowski, pages 305-312).

11. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Stringent hybridization conditions are not described in the specification to definitively and specifically set forth the metes and bounds of the claim. The specification refers to general guidelines that do not set forth a specific number of washes, a specific temperature, a specific ionic strength of the buffer, etc. that would enable the artisan to determine what is encompassed by the claim. Different recombinant nucleic acids would "stringently" hybridize with Clone ATCC 97525 under different specific conditions of washing, temperature, ionic strength, etc. depending on their nucleotide structure, rendering the claim indefinite.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Ullrich et al. ("Ullrich"). Ullrich teaches nucleic acid (Figures 2-3) and fragments (Figure 1) that encode human nerve growth factor (NGF) that possesses the functional property of regenerating neurons, especially sympathetic and sensory neurons (abstract). Since the prior art teaches human nucleic acid that encodes NGF with the functional property recited in the claims, and the specification provides no chemical or structural teachings to distinguish the instant human nucleic acid from the prior art, the prior art is held to be anticipatory, absent evidence to the contrary.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (703) 308-6571. The examiner can normally be reached on Mondays through Thursdays from 0730 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, Ph.D., can be reached on (703) 308-4310. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SG

Stephen Gucker

April 20, 1998

PAULA K. HUTZELL
SUPERVISORY PATENT EXAMINER